

SINGLE-PARTICLE DIFFRACTION IMAGING USING FREE-ELECTRON LASERS

Stefan P. Hau-Riege^{1*},

Henry N. Chapman¹, Anton Barty¹, Michael Bogan¹, Sébastien Boutet^{1,6,7},
Matthias Frank¹, Stefano Marchesini¹, Bruce Woods¹, Saša Bajt¹, Richard A. London¹,
Elke Plönjes-Palm², Marion Kuhlmann², Rolf Treusch², Stefan Düsterer²,
Thomas Tschentscher², Jochen Schneider², Eberhard Spiller³, Thomas Möller⁴,
Christoph Bostedt⁴, Matthias Hoener⁴, David Shapiro⁵, Keith Hodgson⁶,
David van der Spoel⁷, Florian Burmeister⁷, Magnus Bergh⁷, Carl Caleman⁷, Gösta Huldt⁷,
Marvin Seibert⁷, Filipe Maia⁷, Richard W. Lee¹, Abraham Szöke¹,
Nicusor Timneanu⁷, and Janos Hajdu^{6,7}

1 University of California, Lawrence Livermore National Laboratory

2 Deutsches Elektronen-Synchrotron, DESY, Hamburg, Germany

3 Spiller X-ray Optics, USA

4 Institut für Atomare Physik, Technische Universität Berlin, Germany

5 Center for Biophotonics Science and Technology, University of California, Davis

6 Stanford Synchrotron Radiation Laboratory, Stanford Linear Accelerator Center

7 Laboratory of Molecular Biophysics, Institute of Cell and Molecular Biology

Ultrashort coherent x-ray pulses from x-ray free electron lasers (FEL) may enable diffraction imaging of single biological molecules [1]. This would allow the determination of the structure of many molecules that have, to date, resisted crystallization. Radiation damage severely limits image resolution of non-crystalline samples [2]. It has been suggested that extremely short X-ray pulses can be used to image single molecules before the damage takes place. This idea of flash imaging was first suggested by Solem et al. [3], and extended to atomic resolution imaging of single biological molecules by Neutze et al. [1]. It has been shown that atomic-resolution imaging requires extremely short pulses [4].

In a plausible imaging scenario, identical molecules are injected into the x-ray beam in random, unknown orientation and then imaged by a single pulse. The individual 2-D diffraction intensity patterns are then classified according to their similarity, and combined with many other similar patterns. In this way, the patterns of molecules in similar orientation are averaged to increase the signal-to-noise ratio. The averaged diffraction intensity patterns are then assembled into a 3-D diffraction pattern. Finally, a phase-retrieval reconstruction calculation is performed to obtain the 3-D structure of the molecule.

ABSTRACT

Since appropriate light sources will not be available for a few years, design of the biomolecular diffraction imaging experiment has to be done through simulations and modeling. We are testing various aspects of the proposed bio-imaging endeavor through experiments on available synchrotron light sources now, as well as on FELs as they become available.

In this presentation we will discuss venues to alleviate the stringent pulse requirements for biomolecular imaging, including molecular tampers, post-processing of the diffraction patterns, as well as laser-alignment of the particles in the beam. We further describe the results of recent proof-of-principle experiments of flash-diffraction-imaging experiments at the soft x-ray FEL FLASH facility in Germany, providing experimental evidence that with intense ultrafast short-wavelength pulses, structural damage does not occur during the pulse, giving credence to the concept of diffraction imaging of single macromolecules.

* e-mail: hauriegel@llnl.gov

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